GP1632

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Examining Operations

Applicant(s): Kohn, et al.

Serial No: 08/225,478 Art Unit: 1632

Filed: April 8, 1994 Examiner: Campell

Title: Gene Therapy by Administration of Genetically Engineered CD34$^+$ Cells Obtained from Cord Blood

Attorney Docket No.: 271010-211

TRANSMITTAL LETTER

Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

Enclosed please find the following:

1. Response;
2. Declaration Under 37 CFR 1.131 of Donald B. Kohn, R. Michael Blaese, Craig A. Mullen and Robert C. Moen, with Exhibit 1 attached; and
3. A self-addressed, postage paid, return receipt postcard, date stamp and return of which is respectfully requested.

The Commissioner is authorized to charge payment of any additional filing fees required under 37 C.F.R. 1.16 associated with this communication or credit any overpayment to Deposit **Account No. 03-0678**.

FIRST CLASS CERTIFICATE

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Raymond J. Lillie 3/15/99

Raymond J. Lillie, Esq. Date

Respectfully submitted,

Raymond J. Lillie

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#14500 v1 - Gene Therapy Obtained by Cord Blood

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Kohn, et al.

Serial No.: 08/225,478

Filed: April 8, 1994

For: Gene Therapy by Administration of Genetically Engineered $CD34^+$ Cells Obtained from Cord Blood

Group: 1632

Examiner: Campell

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Reconsideration of the above-identified application is hereby respectfully requested.

Accompanying this response is a Declaration Under 37 CFR1.131 of Donald B. Kohn, R. Michael Blaese, Craig A. Mullen, and Robert C. Moen, the co-inventors of the claimed subject matter of the above-identified application. In such Declaration, Drs. Kohn, Blaese, Mullen, and Moen state that, prior to the publication of the Moore and Moritz references, they, or others acting on their behalf, obtained cord blood from two infants suffering from severe combined immune deficiency. $CD34^+$ cells then were isolated from the cord blood of each infant by contacting blood cells with an antibody known as 12.8, which recognizes CD34, and the autologous $CD34^+$ cells were transduced with the retroviral vector LASN. This vector includes a cDNA sequence encoding ADA. The transduced autologous $CD34^+$ cells then were administered to each infant.

Also accompanying this response is a copy of the Valley Edition of the Los Angeles Times of Sunday, May 16, 1993, in which it is stated that one of the patients, Andrew Gobea,

mentioned in Exhibit 1 attached to the Declaration, was given autologous CD34+ cells obtained from his cord blood at birth, wherein the autologous CD34+ cells were infected with a mouse leukemia virus that includes the ADA gene.

Thus, Applicants have shown that the claimed invention was reduced to practice before the publication of the Moritz and Moore references. Therefore, Moritz and Moore are not effective references against the claimed subject matter of the above-identified application.

The remaining references, Anderson, Kohn, and Boyse, as stated previously, do not disclose or even remotely suggest to one of ordinary skill in the art how to obtain $CD34^+$ cells from cord blood of a human. Therefore, Anderson, Kohn, and Boyse do not even remotely suggest to one of ordinary skill in the art that one can express a therapeutic agent in a human autologous $CD34^+$ cells obtained from cord blood, which have been genetically engineered to include a nucleic acid sequence encoding a therapeutic agent. Therefore, the cited prior art does not render Applicants' claimed method obvious to one of ordinary skill in the art, and it is therefore respectfully requested that the rejection under 35 U.S.C. 103 be reconsidered and withdrawn.

Regarding the rejection under 35 U.S.C. 112, first paragraph, the Examiner has admitted that the specification is enabling for genetically engineering $CD34^+$ cells obtained from cord blood with the ADA gene, and administering such $CD34^+$ cells to the patient, whereby ADA is expressed in the patient. The Examiner has not shown that one skilled in the art could not genetically engineer autologous $CD34^+$ cells obtained from cord blood with genes other than the ADA gene, and administer such genetically engineered cells to a human in order to express therapeutic agents other than ADA in the human. The Kohn (1995) and Orkin references cited by the Examiner merely state that further work needs to be done with respect to engineering $CD34^+$ cells with genes other than ADA, and that problems remain in various aspects of gene

therapy. Such references do not state that the various problems associated with gene therapy cannot be overcome, or that $CD34^+$ cells cannot be genetically engineered with genes other than the ADA gene. In fact, the Orkin reference provides a reasonable expectation that gene transfer will be successful for expressing a variety of therapeutic agents. Therefore, the Examiner has provided insufficient evidence for maintaining a rejection under 35 U.S.C. 112, first paragraph, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112 first paragraph, be reconsidered and withdrawn.

For the above reasons and others, the application is in condition for allowance, and it is respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,

Raymond J. Lillie

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(Date of Deposit)
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